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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,720	05/14/2001	Pierre Casellas	IVD 1087	9971

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EXAMINER

SRIVASTAVA, KAILASH C

ART UNIT PAPER NUMBER

1651

DATE MAILED: 04/22/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/831,720

Applicant(s)

CASELLAS ET AL.

Examiner

Dr. Kailash C. Srivastava

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on January 30/2003 as Paper Number 12.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-41 is/are pending in the application.
- 4a) Of the above claim(s) 18,28,37 and 39-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16,17,19-27,29-36 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☒ Interview Summary (PTO-413) Paper No(s) 10.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Applicants' response filed January 30, 2003 as Paper Number 12 to election requirement in Office Action mailed September 27, 2002 as paper number 9 is acknowledged and entered.
2. Claims 16-41 are pending.

Restriction/Election

3. Applicants' election without traverse of Group I, Claims 16-38 filed January 30, 2003 as Paper Number 12 to election requirement in Office Action mailed September 27, 2002 as paper number 9 is acknowledged and entered. Applicants' election, filed January 30, 2003 as Paper Number 12 of fermentation as species for prosecution of this application in response to Office Action dated September 27, 2002 as paper number 9 is also acknowledged. Since the election is made without traverse, the restriction requirement is deemed proper and is made FINAL.

Accordingly, Claims 18, 28, 37 and 39-41 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. Claims 16-17, 19-27, 29-36 and 38 are examined on merits.

Information Disclosure Statement

5. Applicants' Information Disclosure (i.e., IDS) filed May 14, 2001 as paper number 3 has been made of record and is considered.

Priority

6. Applicants' claim for foreign priority under 35 U.S.C. 119 (a-d) is acknowledged.

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 20, 30 and 38 are rejected under 35 U.S.C. § 112, first paragraph, as

containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to actinomycetes: *Actinosynnema* SRL 5189, *Nocardia* SRL 4988 and *Streptomyces* SRL 5186 that produce by fermentation the substance that binds to the peripheral benzodiazepine receptor.

9. Actinomycetes: *Actinosynnema* SRL 5189, *Nocardia* SRL 4988 and *Streptomyces* SRL 5186 are essential to the invention recited in those claims. Those actinomycetes must therefore be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism (s) is not so obtainable or available, a deposit of the microorganism (s) in a recognized depository may satisfy the requirements of 35 U.S.C. §112.

Applicants have made a deposit because they have provided an accession number. However, in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

- (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
- (d) the deposit will be replaced if it should ever become inviable.

Applicant is directed to 37 CFR § 1.807 which states:

(b) A viability statement for each deposit of a biological material defined in paragraph (a) of this section not made under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure must be filed in the application and must contain:

- (1) The name and address of the depository;
- (2) The name and address of the depositor;
- (3) The date of deposit;

- (4) The identity of the deposit and the accession number given by the depository;
- (5) The date of the viability test;
- (6) The procedures used to obtain a sample if the test is not done by the depository; and
- (7) A statement that the deposit is capable of reproduction.

Applicant is also directed to 37 CFR § 1.809(d) which states:

(d) For each deposit made pursuant to these regulations, the specification shall contain:

- (1) The accession number for the deposit;
- (2) The date of the deposit.

Claim Rejections - 35 U.S.C. § 103

10. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

12. Claims 16-17, 19-27, 29-36 and 38 are rejected under 35 U.S.C. § 103 (a) as obvious over Friedman et al. (U.S. Patent 6,004,556) and Glick et al. (U. S. Patent Application Publication 2001/0016583) in view of Komatsu (U. S. Patent 4,011, 140) and Higashide et al. (JP 54073195, English Abstract).

Claims recite a topical composition comprising as active principle, a substance that binds to the peripheral benzodiazepine receptors, wherein said substance is a peripheral benzodiazepine receptor agonist and said agonist is a synthetic molecule, or is extracted substance or a substance obtained by fermentation. Said fermentation is fermentation of

Nocardia or *Streptomyces*. Said composition additionally comprises a retinoid. Claims further recite topical administration of said topical composition to treat cutaneous stress.

Friedman et al. disclose (Column 3, Lines 15-27) topical application of a composition comprising benzodiazepine and a retinoid to treat a skin condition having dermatological diseases/ conditions (e.g., psoriasis, atopic dermatitis). A dermatological condition inherently exerts a stress on skin (i.e., cutaneous stress). Therefore, Friedman et al. teach a composition and a method to treat cutaneous stress. Friedman et al, however, do not disclose that benzodiazepine is a peripheral benzodiazepine receptor agonist. Glick et al. teaches that benzodiazepines have an affinity to peripheral benzodiazepine receptors (Paragraph 0015, Lines 1-7). Thus, Glick et al. remedies the deficiency in teachings from Friedman et al that benzodiazepine is a peripheral benzodiazepine receptor agonist. Please note that skin wrinkles are also a dermatological condition and therefore the prior art reference intrinsically teach to treat wrinkles or other skin stresses through administering Friedman et al's composition.

It would have been obvious to one of ordinary skill in the art at the time the invention was made that benzodiazepine is a peripheral benzodiazepine receptor agonist and the artisan would have topically administered a composition comprising benzodiazepine and retinoid to treat cutaneous stress in an individual based on the teachings of Friedman et al. and Glick et al., because Glick et al. teaches that benzodiazepine is a peripheral benzodiazepine receptor agonist and Friedman et al teach a topical composition, and a method to treat cutaneous stress by topically administering a composition comprising benzodiazepine and retinoid.

None of the previously cited prior art references, however, disclose that the benzodiazepine is produced by fermentation of *Nocardia* or *Streptomyces*.

Higashide et al. (JP 54073195, English Abstract) teach that tobramycin having a benzodiazepine structure is produced by culturing *Nocardia* (Abstract, Lines 4-6). Said abstract, however, does not teach that benzodiazepine is also produced by fermenting *Streptomyces*.

Komatsu teaches that *Streptomyces* fermentatively produces benzodiazepines (Abstract, Lines 1-9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Friedman et al's composition according to the teachings from Higashide et al's English Abstract and Komatsu because each one of the latter prior art references beneficially teach that benzodiazepine is obtained from fermenting each of *Streptomyces* and *Nocardia* respectively. Thus, the English Abstract of Higashide et al. (Abstract Lines 4-6) and Komatsu (Abstract, Lines 1-9) remedy the deficiency in teachings of Friedman et al. of fermentatively produced benzodiazepine through fermentation of each one of *Streptomyces* and *Nocardia*.

One having ordinary skill in the art would have been motivated to modify the teachings from Friedman et al., in view of teachings from Glick et al., Komatsu and English Abstract of Higashide et al., because while Friedman et al. teach a topical composition comprising benzodiazepine and retinoid and a method to administer said composition to treat cutaneous stress, Glick et al. teach that benzodiazepine is a peripheral benzodiazepine receptor agonist. Glick et al. further teach administration of a topical composition comprising benzodiazepine to ameliorate dysfunctional cell death and Komatsu and English Abstract from Higashide et al. teach fermentative production of benzodiazepine through fermentation of *Streptomyces* and *Nocardia* respectively. Thus, Glick et al. remedy deficiency in teachings from Friedman et al. about benzodiazepine being a peripheral benzodiazepine receptor agonist and Komatsu and English abstract from Higashide et al. remedy the deficiency about fermentative preparation of benzodiazepine from *Streptomyces* and *Nocardia*.

None of the above discussed prior art references teach the exact same concentrations of benzodiazepine (i.e., peripheral benzodiazepine receptor agonist). However, the adjustment of particular conventional working conditions (e.g., the quantities of each one of components in a composition and proportions of different components) is deemed merely a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.


Conclusion

13. No Claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (703) 605-1196. The examiner can normally be reached on Monday-Thursday from 7:30 A.M. to 6:00 P. M. (Eastern Standard Time or Eastern Daylight Saving Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


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April 18, 2003



CHRISTOPHER R. TATE
PRIMARY EXAMINER